

Sensor Fabrication and Characterization

ZB Zhenan Bao AA Alex Abramson

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A flexible electronic strain sensor for the real-time monitoring of tumor regression

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Detailed protocol

Supplementary Figure S1 details the scale and the fabrication process for the sensor backpack and the sensor. Sensors were fabricated on a 5.0 cm-by-7.5 cm glass slide (Fisher Scientific, Waltham, USA). As an anti-stick coating, a Micro-90 solution (Cole-Parmer, Vernon Hills, USA) was coated on a slide by spin-coating 300 μ l of solution on the slide at 600 rpm for 20 s. A WS-650MZ-23NPP spin-coater from Laurell Technologies (North Wales, USA) was used. Solutions of SEBS (33 and 50 mg/ml; Asahi Kasei, 1221, Chiyoda City, Japan) in cyclohexane (Fisher Scientific) were generated, and the solution was mixed overnight. The SEBS solution was then drop-casted on a 3 inch-by-2 inch glass slide. To create the 28- μ m-thick substrate, 4 ml of solution at 33 mg/ml was used. To create the 41- μ m-thick substrate, 4 ml of solution at 50 mg/ml was used. To create the 72- μ m-thick substrate, 4 ml of solution at 50 mg/ml and 2 ml of solution at 33 mg/ml were combined and used. A transparency film (ACCO Brands, Boonville, USA) mask was mechanically cut using a Cricut machine (South Jordan, USA) from a mask designed in SolidWorks (Dassault Systèmes, Vélizy-Villacoublay, France). The sensor design consisted of an 11 mm-by-1.5 mm strip, book ended by 3 mm-by-3 mm connection pads. Once cut, the transparency film was sprayed with a nonstick Teflon spray (DuPont, Eleutherian Mills, USA) and placed on the SEBS substrate. Then, a 50-nm layer of gold was deposited on the SEBS at 0.6 Å/s using a metal evaporator from Thermionics Laboratory Inc. (Hayward, USA). Gallium-indium eutectic (Sigma-Aldrich, St. Louis, USA) was placed on the connection pads, and a 30-gauge multicore wire (McMaster-Carr, Elmhurst, USA) was attached to the connection pad using paper tape. The wires were then soldered to a custom-designed PCB (see fig. S3) assembled by DigiCom Electronics (Oakland, USA). The circuit board is powered by a 150-mA-hour lithium-ion rechargeable battery (Digi-Key, Thief River Falls, USA). When awake, the average current draw for the circuit board is 3.5 mA. The sensor backpack (see fig. S1) was printed in three pieces on a Formlabs Form 2 printer (Somerville, USA). The two rigid rods (pictured in light grey) were printed in either rigid resin or gray resin, while the flexible base (pictured in dark grey) was printed in flexible resin. The rigid printed circuit board (pictured in green) and the battery can be placed above the lips of the rigid rods. A scale bar is provided in the picture to denote the sizes of each of the parts. The extended lips on the rigid rods are used to attach the sensors. Note that the small loops in the flexible base can have tissue glue applied to them to allow for initial placement of the backpack. Then, Tegaderm can be wrapped around the animal to hold the sensor in place. This backpack was designed to enable a tumor to grow unencumbered to a diameter of 17 mm, but the backpack can easily be scaled to become larger or smaller.

To measure the resistance of the sensor during stretching, we attached samples to a homemade stretching station and connected the samples to an LCR meter (Keysight Technologies, E4980, Santa Rosa, USA). The stretching station is made of a stepper motor that propels a moving platform forward. The stretching station was controlled by LabVIEW (National Instruments, Austin, USA) and was accurate to step changes as small as 10 micrometers. Before beginning the measurements, sensors were stretched to 200% strain by hand more than 20 times. Samples were then stretched on the stretching station between 0 and 100% strain at 1% intervals, approximately 120 μ m per step, and resistance measurements were recorded in LabVIEW. Following this test, the samples were then stretched to 50% strain, and the resistance of the sensor was measured over the course of 45 min. This test demonstrated that although the sensor underwent relaxation over time, much of the relaxation occurred within the first 45 min (see fig. S1). After this test, the sensor was then stretched from 50 to 60% strain at 0.083% intervals, approximately 10 μ m per step.

To measure the force required to strain the sensor to a given length, we attached the samples to an Instron 5565 (Norwood, USA). We stretched the samples at a rate of 50 mm/min, zeroing the displacement and the force once the sample reached 0.05-N force. Forces were recorded using a 100-N force gauge provided by Instron and read out on the machine's accompanying software. Each sample was stretched until its breaking point.

To measure the thickness of each sensor, we used a Bruker DektakXT-A profilometer (Billerica, USA) and took the average of 10 different readings from multiple sensors taken from various locations on the sensor. The edges of the sensor tended to have a slightly thicker measurement compared to the center of the sensor, leading to a slight variability in thickness readouts (see fig. S1).

To measure the ability of FAST to read out the variation in volume of different shapes, we 3D printed ellipsoid shapes cut in half down their center line. All ellipsoids were scaled linearly and had heights between 2.5 and 5.6 mm, as measured using calipers. These shapes were designed in SolidWorks and printed on an Ultimaker 3 using Ultimaker PLA filament (Geldermalsen, Netherlands). The FAST devices were placed on the shapes, and the sensors were allowed to relax for 20 s before the resistance measurement was recorded.

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1. Bao, Z. and Abramson, A. (2022). Sensor Fabrication and Characterization. Bio-protocol Preprint. [bio-protocol.org/prep2079](https://doi.org/10.1101/207979).
2. Abramson, A., Chan, C. T., Khan, Y., Mermin-Bunnell, A., Matsuhisa, N., Fong, R., Shad, R., Hiesinger, W., Mallick, P., Gambhir, S. S. and Bao, Z. (2022). A flexible electronic strain sensor for the real-time monitoring of tumor regression. Science Advances 8(37). DOI: [10.1126/sciadv.abn6550](https://doi.org/10.1126/sciadv.abn6550)

